UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

DATE: 28 JULY 2006

SUBJECT: **FIPRONIL** - Nondietary Human Exposure/Risk Assessment for the Use of Fipronil as a Pine Seedling Soil Injection.

PC Code: 129121 DP Code: 329997

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INTRODUCTION

Under provisions in § 3 of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) as amended, the BASF Corporation has requested registration of the insecticide fipronil for use as a pine seedling soil injection. This memorandum serves as the HED's assessment of exposures and risk to occupational pesticide handlers (mixers, loaders, applicators).

USE PATTERN SUMMARY

The product proposed for use is BASF PTM SC insecticide (currently not registered). The product is a soluble concentrate liquid formulation which contains 0.8 lb active ingredient (ai) per gallon. The rate of application is 21 fl oz formulation/A (0.13 lb ai/A). There will be one application per year. Application is made by a hand-held device that holds approximately 3 L of solution. The application device might vaguely be likened to a garden watering can with the spout end pointed down towards the ground. When the "spout" end is placed on the ground next to a seedling and the device is pressed, 0.1 - 1.0 fl oz of solution is injected into the soil to a depth of about 3 inches. There is no "spray".

OCCUPATIONAL PESTICIDE HANDLER EXPOSURE

For the proposed use pattern, HED believes occupational handlers may 1) mixer/load a stock solution, 2) "apply" the solution using the hand-held injector or 3) may mix, load and apply the material. Typically for most agricultural and forestry situations, HED relies on exposure data in the Pesticide Handlers Exposure Database (PHED) to characterize exposure to pesticide compounds as the result of using various pesticide formulations and methods of application.

Except for mixing and loading (i.e., preparation of) a minibulk stock solution, there are no PHED exposure data that are directly related to the "application" activities for the proposed use pattern. In situations such as this, if possible, HED utilizes surrogate data that is to say, data that most closely approximate a given exposure situation.

In partial support of the request for registration, the BASF Corporation submitted MRID No. 468385-01 which is an occupational handler exposure assessment ("Fipronil: Mixer/Loader and Applicator Exposure Assessment for Soil Injection Applications to Pine Seedling", by V. Canez, 31 March 06). The BASF assessment utilized surrogate exposure scenarios, taken from the PHED, to estimate occupational pesticide handler exposure and risk. BASF utilized standard HED assessment methodologies found in the EPA OPPTS Harmonized Test Guidelines Series 875 for Occupational and Residential Exposure.

BASF used standard techniques for assessing mixer/loader exposure as noted earlier in this document. BASF then suggests using mixer/loader/backpack sprayer data as one method to assess a "worse case" exposure. HED notes that there is no "spraying" involved with the soil injection application methodology. In addition the soil injector is hand-held, not carried on one's back like a back-pack sprayer. Therefore, HED suggests it is not an appropriate surrogate.

As another surrogate, BASF uses soil injection of pesticide as practiced by persons applying termiticides to the soil. HED believes this much more closely approximates the exposure that would occur using the pine seedling soil injector. However, the volume of material applied during termiticide injection is much greater than what can be handled per day during soil injection for pine seedlings. Therefore, use of the PHED unit exposure data for termiticide soil injection is likely to overstate the exposure experienced by persons using the soil injector to treat pine seedlings.

BASF assessed short-term duration (1 - 30 days) exposures as well as intermediate-term duration exposures (1 - 6 months). HED believes it is unlikely that occupational handlers would experience intermediate-term exposures with this type of use pattern and with the acreages typically involved with pine seedling plantations and reforestation activities.

The BASF assessment includes an adjustment of 1.0 % for dermal absorption. In the HED's most recent assessment of fipronil, (B. Hanson, DP Codes, 316795, 322527, 322529, Memo 15 NOV 2005) the short-term duration (1-30 days) and intermediate-term duration (1 - 6 months) dermal toxicological No Observable Adverse Effect Levels are each 5.0 mg ai/kg bw/day as were used by BASF. However, the NOAELs are identified from a 21-day dermal toxicity study in the rabbit. The toxicological effects noted were decreased body weight gain and food

consumption in both sexes. It should be noted that since the NOAELs are identified from a dermal toxicity study, it is not necessary to correct for dermal absorption. Therefore, HED utilizes portions of the BASF assessment such as "units treated" but does not correct for dermal absorption.

The HED's 15 November review cites short- and intermediate-term inhalation toxicological endpoints as well. The NOAELs are 0.05 mg ai/kg bw/day and are identified from a developmental neurotoxicity study in the rat. The toxic effects were decreases in mean pup weights during lactation and significant increase in time of preputial separation in males. Since the inhalation toxicological endpoints are identified from a developmental study with fetal effects, a body weight of 60 kg is used to calculate inhalation exposure. See the ATTACHMENT for a summary of the toxicological endpoints used for purposes of risk assessment.

BASF indicates workers may treat 3,000 trees/day at a planting density of 500 trees/A. That equates to 6 A/day that may be planted. The rate of application is 0.13 lb ai/A therefore approximately 0.78 lb ai are handled per day. The remainder of the assessment utilizes standard HED procedure.

Unite Exposure (PHED)	*	Amount ai handled/day (BASF assessment)	÷	Body weight (70 kg for dermal 60 kg for inhalation)

Since the toxicological effects are determined from different studies and cite different effects, the Margins of Exposure (MOE) are combined in the following fashion.

$1/\ 1/MOE_{dermal} + 1/MOE_{inhalation}$

For a mixer/loader wearing protective gloves using open pour loading of liquids:

Dermal
0.023 mg/lb ai handled * 0.78 lb ai handled/day ÷ 70 kg bw = 0.000256 mg ai/kg bw/day

MOE = NOAEL ÷ exposure therefore, 5.0 mg ai/kg bw/day ÷ 0.000256 mg ai/kg bw/day = 19,531

Inhalation
0.0012 mg/lb ai handled * 0.78 lb ai handled/day ÷ 60 kg bw = 0.0000156

MOE = 0.05 mg ai/kg bw/day ÷ 0.0000156 mg ai/kg bw/day = 3,205

Combined MOE = 2,753

For a mixer/loader/applicator wearing protective gloves and performing soil injection for termite control:

Dermal
0.36 mg/lb ai handled * 0.78 lb ai handled/day ÷ 70 kg bw = 0.00401 mg ai/kg bw/day

MOE = 5.0 mg ai/kg bw/day ÷ 0.00401 mg ai/kg bw/day = 1,246

Inhalation
0.0022 mg/l bai handled * 0.78 lb ai handles/day ÷ 60 kg bw = 0.0000286

MOE = 0.05 mg ai/kg bw/day ÷ 0.0000286 mg ai/kg bw/day = 1,748

Combined MOE = 727

A MOE of 100 is adequate to protect occupational pesticide handlers. Since the estimated MOEs are > 100, the proposed use does not exceed HED's levels of concern.

POST-APPLICATION EXPOSURE

Typically, there is the possibility for agricultural (or forestry) workers to experience post-application exposures to dislodgeable pesticide residues. For the proposed use pattern, HED expects that the only post-application activity that might occur is scouting for plant stand efficiency (i.e., how well the planted stand is progressing) and by default, for pesticide efficacy. In this case the pesticide in injected below the soil surface and scouting is not likely to occur within days after planting, therefore HED considers post-application exposure to be negligible and an assessment of post-application exposure is not necessary. The proposed use pattern does not exceed HED's level of concern. Further, it is not necessary to consider a restricted entry interval (REI) since there is essentially no post-application exposure.

ATTACHMENT

Summary of Toxicological Dose and Endpoints for Fipronil for Use in Human Risk Assessment [1].

Exposure Scenario (Fipronil)	Dose Used in Risk Assessment, UF	FQPA SF and Endpoint for Risk Assessment	Study and Toxicological Effects
Acute Dietary all populations including infants and children	NOAEL= 2.5 mg/kg UF = 100 **Acute RfD** = 0.025 mg/kg	FQPA SF = 1 **aPAD** = acute RfD / FQPA SF = 0.025 mg/kg	Acute neurotoxicity - rat LOAEL = 7.0 mg/kg based on: decreased hindleg splay in males at 7 hours.
Chronic Dietary all populations	NOAEL= 0.019 mg/kg/day UF = 100 **Chronic RfD** = 0.0002 mg/kg/day	FQPA SF = 1 **cPAD** = chr RfD / FQPA SF = 0.0002 mg/kg/d	Chronic/carcinogenicity study - rat LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4.
Short-Term Oral (1-7 days) (Residential)	oral study LOAEL ≤0.1 mg/kg/day UF of 3 for no NOAEL, 100 for interspecies extrapolation and intraspecies variation	**LOC for MOE** = 300 (Residential, includes the FQPA SF)	Developmental toxicity Study - rabbit LOAEL = ≤ 0.1 mg/kg/day based on: maternal toxicity of decreased body weight gain, decreased food consumption, and decreased food efficiency.
Intermediate-Term Oral (1 week - several months) (Residential)	oral study LOAEL ≤0.1 mg/kg/day UF of 3 for no NOAEL, 100 for interspecies extrapolation and intraspecies variation	**LOC for MOE** = 300 (Residential, includes the FQPA SF)	Developmental Toxicity Study - rabbit LOAEL = ≤ 0.1 mg/kg/day based on: maternal toxicity of decreased body weight gain, decreased food consumption, and decreased food efficiency.
Short-Term Dermal (1-7 days) (Occupational/ Residential)	dermal study NOAEL= 5 mg/kg/day	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes FQPA SF)	21-Day dermal toxicity study - rabbit LOAEL = 10.0 mg/kg/day based on: decreased body weight gain, and food consumption in both sexes.
Intermediate-Term Dermal (1 week - several months) (Occupational/ Residential)	dermal study NOAEL= 5 mg/kg/day	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes FQPA SF)	21-Day dermal toxicity study - rabbit LOAEL = 10.0 mg/kg/day based on: decreased body weight gain, and food consumption in both sexes.

Summary of Toxicological Dose and Endpoints for Fipronil for Use in Human Risk Assessment [1].

Exposure Scenario (Fipronil)	Dose Used in Risk Assessment, UF	FQPA SF and Endpoint for Risk Assessment	Study and Toxicological Effects
Long-Term Dermal (several months - lifetime) (Occupational/ Residential)	oral study NOAEL= 0.019 mg/kg/day (dermal absorption rate = 1%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes FQPA SF)	Chronic/carcinogenicity study - rat LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4.
Short-Term Inhalation (1-7 days) (Occupational/ Residential)	oral study NOAEL= 0.05 mg/kg/day (inhalation absorption rate = 100%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes FQPA SF)	Developmental neurotoxicity - rat LOAEL = 0.90 mg/kg/day based on: decrease in group mean pup weights during lactation, and significant increase in time of preputial separation in males (dietary).
Intermediate-Term Inhalation (1 week - several months) (Occupational/ Residential)	oral study NOAEL= 0.05 mg/kg/day (inhalation absorption rate = 100%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes FQPA SF)	Developmental neurotoxicity - rat LOAEL = 0.90 mg/kg/day based on: decrease in group mean pup weights during lactation, and significant increase in time of preputial separation in males (dietary).
Long-Term Inhalation (several months - lifetime) (Occupational/ Residential)	oral study NOAEL= 0.019 mg/kg/day (inhalation absorption rate = 100%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes FQPA SF)	Chronic/carcinogenicity rat study LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4.
Cancer (oral, dermal, inhalation)	Group C - possible human carcinogen	Use chronic RfD to estimate human risk	Increases in thyroid follicular cell tumors with fipronil (male/female)

[1] UF = uncertainty factor, FQPA SF = FQPA Safety Factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, LOC = level of concern, MOE = margin of exposure.

NOTE: The ATTACHMENT is taken from: (B. Hanson, DP Codes, 316795, 322527, 322529, Memo 15 NOV 2005, "Petition Number: 05OR18 - **Human Health Risk Assessment for Fipronil** - Incorporating the Section 18 Proposal for the Use of Fipronil on Turnips and Rutabagas in Oregon and the Renewal Request for use of Fipronil on Corn.").

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Chemical: Fipronil

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